Current Approaches to Pediatric Polyposis Syndromes

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Abstract

Colorectal adenomatous polyposis syndromes encompass a diverse group of disorders with varying modes of inheritance and penetrance. Children may present with overt disease or within screening programs for families at high risk. We provide an overview of the array of pediatric polyposis syndromes, current screening recommendations, and surgical indications and technical considerations. Optimal disease management for these pediatric patients is still evolving and has implications for screening, surveillance, pediatric surgical management, and transition of care gastroenterologic neoplasia physicians and surgeons.

Keywords
- IPAA
- pediatric polyposis
- restorative proctocolectomy

Polyp syndromes derive from adenomatous, hamartomatous, or hyperplastic polyps. Treatment varies significantly based on the nature and distribution of polyps, disease volume, risk of malignant transformation, and type of gastroenterologic or surgical management.

Adenomatous Polyp Syndromes

Familial Adenomatous Polyposis

Familial adenomatous polyposis (FAP) is the most common of the polyposis syndromes, with an estimated prevalence of 2 to 3 per 100,000 persons across all ethnic groups.[1] It is an autosomal dominantly inherited cancer syndrome characterized by mutations in the gene for adenomatous polyposis coli (APC) and development of hundreds to thousands of colorectal adenomatous polyps.[2] FAP is defined clinically as $\geq$ 100 adenomatous colon and rectal polyps. It typically presents with malignancy or symptoms in patients younger than 40 years. Left untreated, the FAP penetrance for colorectal cancer (CRC) is close to 100% by the age of 50 years.[3]

The *APC* gene spans 108 kb of genomic DNA on chromosome 5.[3] It encodes a tumor suppressor protein that functions by downregulating the β-catenin oncoprotein. In the absence of the APC protein, β-catenin accumulates in the nucleus and leads to the involvement of upregulation of genes in cell cycle entry and dysplasia. More than 400 mutations of the *APC* gene correlate with the clinical phenotype and the severity of manifestations. Classic FAP is associated with other benign and premalignant lesions throughout the gastrointestinal tract, including fundic gland gastric polyps, gastric adenomatous polyps, and small-bowel polyps, as well as periampullary carcinoma.[4]

Attenuated Familial Adenomatous Polyposis Syndromes

Several variants of FAP have different genetic mutations associated with various ages of onset and various CRC risks.

Patients with attenuated AFAP usually have fewer polyps that occur at a later age of onset. In addition, rectal sparing and right-sided adenomas often develop. These patients do not have extracolonic mutations and have a reduced risk of CRC. AFAP arises from mutations in the *APC* gene at either the proximal or distal end or in locations of exon 9.[5]

MUTYH-associated polyposis is the second most common attenuated FAP-related syndrome and involves the *MUTYH* gene —which is active in the repair of DNA damaged by oxidative stress—thereby resulting in transversions in multiple genes, including *APC* and *KRAS*.[6] Biallelic germline mutations in *MUTYH* are known to cause a less severe form of adenomatous polyposis, similar to attenuated FAP, in which the patient typically has less than 100 adenomatous polyps. *MUTYH*-associated polyposis is inherited in an autosomal recessive way, and *MUTYH* mutations have been identified in 7.5 to 12.5% of patients who have more than 100 adenomas without an *APC* mutation.

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Polymerase proofreading–associated polyposis is a recently described syndrome where the phenotype includes a reduced number of polyps (relative to *APC* or *MUTYH*) but with high penetrance, high dysplastic risk, and early progression to CRC.[7] Germline mutations in enzymes encoding the catalytic and proofreading activities of the leading-strand DNA polymerase epsilon (*POLE*) and the lagging-strand polymerase delta (*POLD*) are responsible.[8] Polymerase proofreading–associated polyposis has been reported in up to 7% of families with colorectal adenomas and carcinomas without *APC* or *MUTYH* mutations.[9]

In 30 to 50% of patients with adenomatous polyposis, no germline mutation can be identified in the *APC*, *MUTYH*, or *POLE/POLD1* genes. An *APC* mutational mosaicism may be detected in 11 to 20% of patients. An additional 30 low-susceptibility variants have been identified that increase risk of CRC.[9] Whether a patient carries a genetic susceptibility for cancer is an important determinant of when and how to screen the patient, as well as an indication for their likely response to chemotherapy, and their expected prognosis. Patients with mutational mosaicism or low-susceptibility variants typically received the diagnosis of malignancy at an older age than those who were clear gene carriers, though many of these patients with low susceptibility variants or mutational mosaicism had a strong family history of CRC, conforming to Amsterdam II criteria,[10] and as such were still candidates for prophylactic surgical management of their disease process.

Hamartomatous Polyp Syndromes

Hamartomatous polyps are pedunculated, cherry-red polypoid lesions. Hamartomatous polyp syndromes that increase rates of CRC include Peutz-Jeghers syndrome (PJS), juvenile polyposis syndrome (JPS), and phosphate tension homolog *(PTEN)* hamartoma syndrome.

PJS is an autosomal dominant syndrome. Diagnostic criteria include the presence of $\geq$ 2 hamartomatous polyps anywhere in the gastrointestinal tract, one confirmed hamartomatous polyp in a patient with a family history of PJS, and typical perioral pigmentation.[11] The mutation occurs in a gene that codes for a serine or threonine kinase (*LKB1* or *STK11*), which acts as a tumor suppressor. Varying mutations lead to the phenotypic variability of PJS. The lifetime risk of CRC in PJS has been estimated as 39%, and PJS patients are also vulnerable to pancreatic cancers, breast tumors, and cervical and testicular tumors.[12,13] Management of PJS centers on resection of large polyps and surveillance for malignant tumors. Patients should undergo upper and lower endoscopy biennially after the age of 30 years, and endoscopic resection is recommended for polyps greater than 1.5 cm. Family members also should undergo regular screening.[14]

Juvenile polyposis syndrome is a rare syndrome inherited with incomplete penetrance in 20 to 50% patients with hamartomatous polyps. JPS diagnostic criteria include more than five juvenile polyps in the colon or the rectum, multiple juvenile polyps throughout the entire gastrointestinal tract, and one or more polyps in combination with a family history of juvenile polyposis.[15] Germline mutations have been described in *SMAD4* and *BMPR1* genes in some, but not all, cases of JPS. The most affected sites of polyps in JPS are colon and rectum (98%), stomach (14%), jejunum and ileum (7%), and duodenum (2%).[15] The estimated CRC risk is 17 to 22% by the age of 35 years, though gastric, duodenal, and pancreatic cancers are also common.[16] Depending on location, juvenile polyps should be resected endoscopically or surgically. A prophylactic colectomy has been advocated for patients who have polyps with early adenomatous features, dysplasia, or a family history of CRC.[17] Surveillance of the pouch and ileal mucosa should be ongoing.[18]

PTEN hamartomatous tumor syndromes (PHTSs) include Cowden's syndrome and Bannayan-Riley-Ruvalcaba syndrome. Both of these syndromes are characterized by the autosomal dominant inheritance of mutations in the *PTEN* (phosphatase and tensin homolog) gene, which encodes a tumor suppressor. *PTEN* mutations are found in 25% of patients with PHTS; other patients have *SDH* (succinate dehydrogenase) or *KLLN* (killin) mutations.[19] Mucocutaneous features of trichilemmomas, oral papillomatosis, and feet or hand keratosis are present in 80% of patients with PHTS, whereas colorectal polyps are found in 35 to 65% of patients.[20] CRC risk in PHTS is significantly increased relative to the general population, with a 4- to 10-fold increased risk[21] or an 18% risk of CRC at the age of 60 years.[22] Recommendations are for colonoscopy beginning at the age of 40 years and biannual surveillance with surgical intervention based on disease burden.[18]

Serrated Polyp Syndromes

Of all CRCs, 15 to 30% arise from serrated polyps rather than from adenomatous polyps. Serrated polyposis syndrome (SPS) is characterized by multiple serrated polyps throughout the colon and is accompanied by an increased CRC risk.[23] Because germline mutations for SPS are still unknown, the disease is defined clinically by (1) the presence of five or more serrated polyps proximal to the sigmoid colon, of which two are more than 10 mm in diameter; (2) the presence of one serrated polyp proximal to the sigmoid and a first-degree relative with SPS; or (3) 20 serrated polyps located throughout the colorectum, or a combination of these clinical findings. CRC risk for patients at their first SPS presentation is reported between 29 and 50%; however, this range likely overestimates the risk because of selection bias and nonstructured surveillance.[24] In SPS, CRC is diagnosed at a median age of 60 years.[24] Screening is recommended to begin at the age of 40 years and to continue at a rate of every 1 to 3 years.[18]

Screening and Surveillance

The American College of Gastroenterology has devised recommendations for screening and surveillance for the polyposis syndromes, outlined in ►**Table 1**.[18]

Indications and Overview of Surgical Intervention

Indications

Pediatric indications for colorectal surgery in any of the polyposis syndromes include documented or suspected

Table 1 American College of Gastroenterology Recommendations for age to begin screening and repeat screening interval for pediatric polyposis syndromes[18]

Polyposis syndrome	Age to begin screening, y	Repeat screening interval, y
FAP	10–15	1–2
Attenuated FAP	18–20	1–2
MUTYH-associated polyposis	25–30	1–2
Peutz-Jeghers syndrome	8–18	3
Juvenile polyposis syndrome	12–15	1–3
PTEN hamartomatous tumor syndromes	15	2
Serrated polyposis syndrome	40	2

Abbreviation: FAP, familial adenomatous polyposis.

cancer and symptoms refractory to endoscopic management. Relative indications include the presence of multiple large adenomas, a notable increase in number of adenomas, high-grade dysplasia, or the inability to complete colon surveillance because of multiple diminutive polyps. Deep family concern, particularly when there has been a death due to CRC, may prompt requests for earlier colectomy in otherwise asymptomatic children with a high volume of disease. Planning for major prophylactic surgery must consider the child's input, growth, development, and school life. Colectomy before the teenage years is reasonable in the subset of patients with thousands of polyps and a family history of early-onset cancer.[25]

Surgical management for FAP most often includes a restorative proctocolectomy with ileal pouch anal anastomosis (IPAA).[26] Patients with AFAP may be successfully treated with repeated endoscopic polypectomies and may never need a colectomy, depending on ability to survey the colon and achieve polyp clearance. In addition, some patients with AFAP and *MUTYH*-associated polyposis have relative rectal sparing, allowing ileorectal anastomosis (IRA) rather than IPAA.[5] Both groups need endoscopic monitoring for malignancy within the remaining rectum or at the anal transition zone.[27]

For PJS, endoscopic removal of all polyps is first attempted, but colectomy is sometimes indicated when colonoscopic management is not possible or neoplasia is seen in the colonic polyps.[28] For JPS, colectomy may be indicated when cancer or high-grade dysplasia is detected or when the polyps cannot be adequately controlled endoscopically.[29] In addition, abundant polyp burden can be associated with protein-losing enteropathy, diarrhea, and electrolyte imbalances.

For SPS, development of cancer or high-grade dysplasia or the failure to endoscopically control the serrated polyp growth are indications for surgery. When indicated, prophylactic or therapeutic colectomy is with either subtotal colectomy and IRA or proctocolectomy with IPAA.[30]

Surgical Approach

Prevention of cancer in children with polyposis syndromes is managed most effectively through total colectomy with IRA or by proctocolectomy with IPAA.[31] Proctocolectomy with IPAA is a restorative procedure that minimizes the risk of CRC by removing almost all at-risk mucosa while maintaining reasonable bowel continence.[32] This technique has been widely used in adults since the 1980s but only recently in children.[32] Operative steps include proctocolectomy, endoanal mucosectomy, and IPAA with or without a diverting ileostomy. Originally an open procedure, its use progressed through laparoscopy-assisted technique, and now it is commonly performed laparoscopically.[33,34] It has also been done successfully through a single laparoscopic incision.[35,36]

IRA versus IPAA

A spectrum of opinion still exists among pediatric and colorectal surgeons on the optimal extent of resection for prophylactic surgery in FAP—namely, whether IRA or IPAA is the more suitable prophylactic procedure.[37] IRA was previously considered less invasive, involving less pelvic dissection and associated morbidity and with better functional outcomes than IPAA in selected subsets of patients.[38] Patients with FAP who underwent IRA rather than IPAA had reduced daily bowel frequency, less nocturnal stooling, and fewer 30-day reinterventions.[37] The clear disadvantages of IRA are the need for ongoing surveillance secondary to the risk of CRC in the rectum,[39,40] leading to a secondary proctectomy (42% at 20 years).[40,41] IPAA leaves less mucosa with the potential for dysplasia, which may be further reduced when mucosectomy is performed to undertake a hand-sewn pouch anal anastomosis.[42,43] However, some evidence shows that mucosectomy itself can lead to a worse functional outcome and may carry the risk of leaving islands of mucosa on the muscle cuff hidden from endoscopic surveillance.[43–45]

In some published literature, IRA has been advocated for any patients younger than 30 years, with subsequent conversion to IPAA if indicated after follow-up surveillance.[46] The purported advantage of this approach includes a less complex procedure without the need for a pouch and, importantly for children, a lower risk of infertility and impotence.[47,48] Although IRA is feasible for patients with attenuated FAP, the increasing risk of CRC in the remaining rectum with age is considerable and has been reported at between 29 and 35% at 25 years after the original procedure.[38,46] In that clinical setting, secondary excision of the rectum may be necessary, as reported by Booij et al,[49] where 7 of 34 patients had completion proctectomy and 2 patients died secondary to invasive rectal cancer.[49]

Functionally, there is little choice between IRA and IPAA.[50] Newer studies indicate that laparoscopic approaches may have reduced the effect of IPAA on long-term fertility.[51,52] Furthermore, with the greater complexity of a secondary proctectomy, it may not be possible to convert an IRA into an IPAA, and if such a patient has rectal cancer, then the patient may need a completion proctectomy with end ileostomy rather than a restorative procedure.[41] Thus, despite the increased complexity and potentially increased

morbidity of a proctectomy, IPAA should currently be proposed to any high-risk FAP patient as the operation of choice for optimal control of CRC risk.

Straight versus Pouch Reconstruction

Straight ileoanal anastomoses were initially championed for children because they were thought to be associated with less risk of strictures, less fecal stasis, and less inflammation of the neorectum.[53] They were already used commonly in pediatric surgery techniques involving pull-through for colonic aganglionosis or anorectal malformations. The straight pull-through technique retains the functional direction of peristaltic contractions and can generate physiological spike waves down to the anal anastomosis. The procedure also can be technically simpler than the pouch creation.

Although the high adaptability of children and excellent continence mechanisms were expected to mitigate the problems of high stool frequency,[53] creation of an ileal reservoir was seen to result in superior daily continence and less frequent daily bowel movements compared with the straight pull-through.[54] Ileal pouches are now standard of care for most pediatric reconstructive procedures.[55] Four pouch configurations have been used: lateral, S-shaped, J-shaped, and W-shaped pouches.

The J pouch configuration is favored because of its technical simplicity, quick creation, ease of the fit of the pouch into the sacrum, excellent functional outcomes, and a dearth of long-term complications.[26] Both the S and W pouches are hand-sutured, leading to increased complexity and a longer operating time. The S and W pouches are more vulnerable to outlet obstruction and the need for an irrigating catheter.[56] The lateral reservoir has been infrequently done in recent years, but it may be considered to reduce the tension at the anastomosis in patients with a short ileal mesentery.[57] The first IPAA described by Park and Nicholls[32] involved an S-shaped ileal pouch mobilized through a mucosectomized rectum and hand-sewn to the dentate line. The J pouch, initially described by Utsunomiya and colleagues,[58] has now become the most widely used, being simpler than other techniques, highly functional, and less prone to long-term complications.[55]

To construct the J pouch, the ileal mesentery should be mobilized adjacent to the superior mesenteric vessels in a length sufficient to allow the ileum to be anastomosed to the anus without tension. To create the pouch, the ileum is folded back on itself for a pouch length of 10 to 12 cm, and a stapling device is used to form the anastomosis. Sutures also are placed in a seromuscular manner at the top of the suture line, to divert tension off the area. The length of the J pouch was shortened after the realization that longer pouches led to increased stool stasis and pouchitis.[58]

Straight versus J-Shaped Pouch IPAA

A pediatric meta-analysis comparing the straight IAA versus the J pouch IAA indicated a trend for lower daily stool counts in children who had a pouch rather than a straight pull-through.[59] However, a further multicenter study indicated that although straight anastomosis had higher stool frequency and the J pouch had increased pouchitis at 12 months from surgery, these problems regressed over the next 12 months from surgery and functional stooling scores became similar between the two groups.[55] The patients with J-style pouch anastomoses maintained lower stool frequency and marginally better continence; yet, these differences became small later and may have had minimal clinical significance. Continence stayed excellent regardless of which technique was used (92 vs. 97% at 1 year).[55] Straight anastomosis reduced the risk of pouchitis associated with an ileal reservoir. However, rates of pouchitis were lower in anastomosis undertaken for FAP than for ulcerative colitis (UC), and that incidence itself decreased after 24 months.[55] Pull-through failures requiring reversion to a permanent ileostomy occurred in 6% of patients, and that percentage did not vary with any statistical significance between groups (8% S-shaped IAA [most often secondary to stooling frequency] and 5% J-shaped PAA [most often secondary to pouchitis]).[55]

S-Shaped, J-Shaped, or W-Shaped Pouch

Evaluation has been extensive on the different types of ileal pouch reservoirs.[60–63] Anatomically, a J pouch fits optimally into the sacrum, with the larger end of the J resting on the levators. An S pouch creates a longer spout, which carries the potential to lead to obstruction or kinking. A meta-analysis of 18 studies that contained 1,519 patients—689 with a J pouch, 306 with a W pouch, and 524 S pouch—was not able to detect any statistically significant difference in early postoperative complications.[60] In the short term, daily stool frequency was greater for patients with a J pouch than an S or W pouch.[60] Obstructed evacuation was more common in patients with an S- or W-shaped pouch. No long-term significant difference was detected between patients with an S-shaped pouch and those with a J-shaped one for most functional outcomes.[60] Variation within the patient subset techniques (e.g., hand-sewn vs. stapled and laparoscopic vs. open) and the patient indications (FAP vs. UC) may make it difficult to detect any true difference in outcomes for individual patients. At this time, the risk of obstruction in the S-shaped pouch is further decreased with suggestions that the exit conduit of an S-shaped pouch should be no greater than 2 to 2.5 cm in length, as opposed to 5 cm in its initial designs.[56]

Hand-Sewn versus Stapled Anastomosis

Currently, no consensus exists on whether to undertake hand-sewn anastomosis or stapled anastomosis in children. The IPAA procedure was originally designed to include a rectal mucosectomy and hand-sewn ileal pouch to anal canal anastomosis. By preserving the anal canal transition zone and a cuff of distal rectum, a double-stapled technique was thought to potentially result in improved postoperative function.[64] To this day, though, controversy continues regarding which of these techniques is superior.[65]

The stapled technique (as illustrated in ►**Fig. 1**) is thought to be technically easier and thus has been proposed to be less prone to leak or stenosis complications and to have fewer sepsis-related pouch excisions.[66] However, in patients with FAP, a matched-pair analysis indicated a nonstatistically significant tendency toward a higher rate of early postoperative complications—in particular, stenosis—after stapled IPAA.[67]

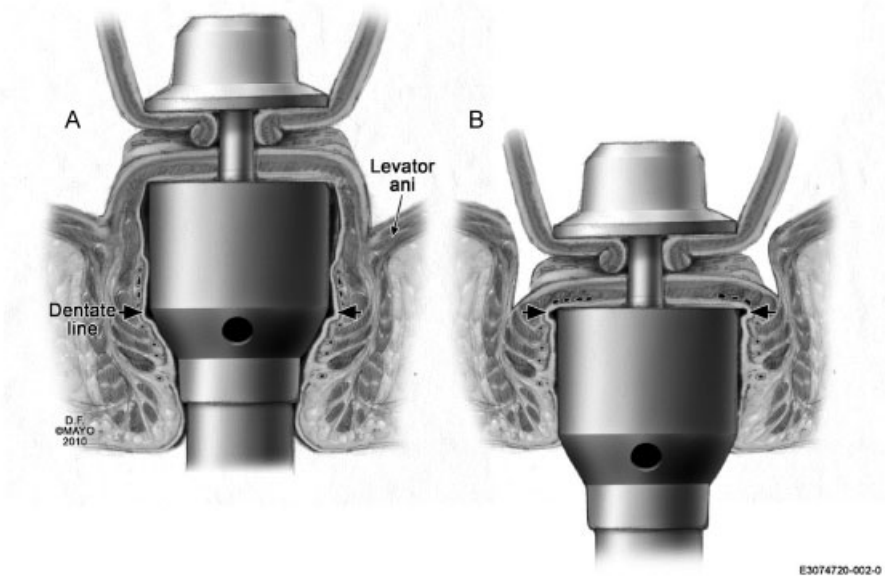

Fig. 1 Stapled ileoanal anastomosis. (**A**) The anastomosis is undertaken with the circular stapler as indicated. (**B**) Shorter cuff lengths are possible with this technique (©Mayo Clinic).

Pouchitis outcomes are seen as comparable between hand-sewn and stapled anastomosis.[68] The stapled technique tends to be undertaken in larger children, in keeping with the adult colorectal experience and with the availability of appropriate sizes of staplers. Stapled anastomosis leads to a longer cuff length, which was hypothesized to improve functional outcomes. However, a meta-analysis of prospective studies did not detect a statistically significant difference in long-term functional outcomes between hand-sewn or stapled anastomosis.[69]

For the UC patient population, recent literature supports a stapled IPAA, with improved functional results and fewer postoperative complications than the hand-sewn anastomosis.[66,68,70] A mucosectomy and hand-sewn IPAA are entirely necessary in certain situations, though: neoplasia in the anal transition zone, large polyp burden in the low rectum, a revision IPAA, and small patient size in a younger patient for whom stapling devices do not fit.[43]

With or without a Diverting Stoma

The restorative proctocolectomy can be performed with or without a diverting loop ileostomy.[25,71] It was initially a standard practice to perform IPAAs as two- or three-stage procedures, in particular using a diverting loop ileostomy to reduce the risk or impact of pelvic sepsis,[72] which is known to be a critical determinant of pouch failure.[73] A North American survey indicated that most colorectal surgeons believed that proximal diversion at the time of IPAA was still indicated.[74] In particular, there is concern that a pelvic complication could lead to pouch failure and create the need for a permanent ileostomy.[75–77] Several studies have shown a low complication rate even with a single-stage approach.[71,78] As such, the incidence of one- and two-stage IPAAs have increased over time and are considered in younger patients particularly.[25] Evaluation of the Mayo Clinic pediatric experience indicated that patients with one-stage procedures had higher rates of leak and higher need for reoperation than patients with two-stage IPAAs.[25] The patients had better long-term bowel function with a one-stage IPAA.[25] Hence, current recommendations cite a diverting ileostomy as the standard of care, with one-stage procedures only in highly selected patients.

Anatomical Reach

Regardless of which pouch technique is chosen, the anastomosis must reach the anus without undue tension. In univariate and multivariate analyses, Heuschen et al[79] showed that anastomotic tension was a significant risk factor for early complications in patients with FAP, in particular for pouch-related septic complications. For a pouch, the site of ileal reach needs to be proximal to the terminal staple line. For instance, for the J-shaped pouch, a site 16 to 20 cm proximal to the terminal ileal staple line is the actual anastomotic ileoanal apex. Therefore, the reach needs to be longer than for a straight pull-through procedure.

The pediatric mesentery is not necessarily more flexible than the adult mesentery; so, mesenteric windows and lengthening maneuvers are necessary to minimize tension on the anastomosis (►**Fig. 2C–E**). Relaxing incisions in the peritoneum can be made both front and back. Typically, approximately five relaxing incisions are made, and these will likely gain up to 2 cm in length.[80]

The main feature limiting reach is the mesenteric vessels, some of which need to be sacrificed to optimize reach and minimize tension (►**Fig. 2A**). Initial studies by Smith et al[81] identified key principles that should be observed during the management of the mesenteric circulation. By dividing the distal superior mesenteric artery but preserving the ileocolic artery, an extra 2.5 cm in length on average could be generated. Martel et al[82,83] analyzed whether a high division of the superior mesenteric artery with preservation of the ileocolic artery was safe. They showed that this approach led to an increased reach of 3.5 cm on average and often necessitated a longer ileal resection. Burnstein et al[80] stated that division of

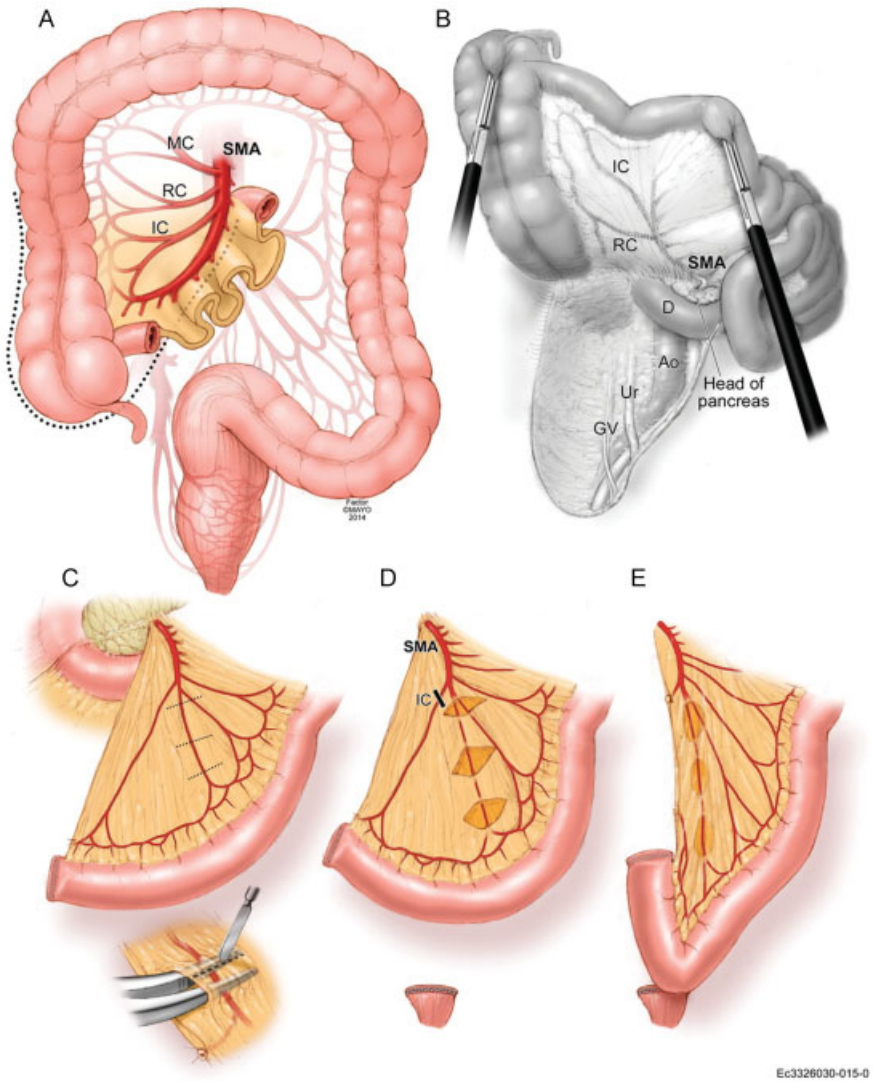

Fig. 2 Maneuvers to increase mesenteric reach in ileal pouch anal anastomosis. (**A**) Initial mobilization of the ileal mesentery away from the retroperitoneum by optimal dissection to the mesenteric root of the SMA (IC artery, ileocolic artery; RC, right colic artery; –MC, middle colic artery). (**B**) This exposes the aorta (ao), duodenum (D), right ureter (Ur), and gonadal vessels (GV). (**C**) The mesenteric reach can be further extended by scoring the peritoneum stepwise. (**D** and **E**) Ligation of the ileocolic with preservation of the distal SMA can provide further reach for the ileal J pouch (©Mayo Clinic).

either of the major mesenteric vessels was usually unnecessary, particularly in the pediatric population. Their technique, instead, involved division of two or three smaller ileal mesenteric arteries between the primary and secondary arcades, resulting in an average of 2 to 5 cm of extra length.[80] An alternative technique if reach is a more challenging involved preservation of the right branch of the middle colic and the marginal artery of the right colon with division of the right colic and ileocolic arteries at their origin. An average extra 11 cm was gained through this technique.[84] Cherqui et al[85] showed that mobilization to the mesentery root added 1 cm in some patients[85] (►**Fig. 2B**). These techniques can be used in combination with optimized reach, depending on the patient's anatomy.[86]

Laparoscopic versus Open Approach

Minimally invasive laparoscopic approaches for these young and asymptomatic patients are appealing. All currently published reports indicate that laparoscopic restorative proctocolectomy is safe and may result in a shorter length of hospital stay and a better cosmetic outcome.[33] The drawbacks that investigators observed include longer operating times initially and a steep learning curve. With technique improvement, better outcomes, including reduced adhesions, less postoperative pain, and ileus, and a quicker return to normal activities may emerge for laparoscopic IPAA.[87–89] In addition, single-port laparoscopic approaches are being innovated to further advance minimally invasive management for this young patient population.[35,36]

Contraindications to IPAA

Absolute contraindications to IPAA are few. Occasionally, when the mesentery is foreshortened, a restorative surgery is unable to proceed despite mesenteric lengthening procedures. This result is particularly the case for patients with a thick mesentery and a high body mass index. Malrotation, recurrent desmoid tumors, and prior hepatoblastoma surgery are all relative

contraindications to proceeding to IPAA but not to proceeding to colectomy and end ileostomy. Similarly, rectal dysplasia mandates a full proctectomy with mesorectal excision rather than an IPAA.[90] Children or young adults with rectal dysplasia or malignancy will reasonably resist permanent ileostomy as the only option, but the procedure should not be delayed when indications to operate are strong. Judgment is of course paramount. A patient at high risk for desmoid tumors should not undergo early prophylactic IPAA. However, with the nearly 100% incidence of invasive adenocarcinoma by the age of 50 years, concerns for desmoid complications, while important, are outweighed by the cancer risk in otherwise healthy patients.

The decision to operate continues to be based on cancer prophylaxis. When familial patterns and genotype identify high-risk patients and surveillance confirms imminent malignancy, colectomy should proceed despite the relative contraindications of a permanent ileostomy.

IPAA Morbidity and Long-Term Outcomes

Overall, morbidity from prophylactic IPAA is substantial and ranges from 10 to 25% for patients with FAP—notably better than for patients undergoing surgery for UC.[91,92] Anastomotic leak and sepsis range from 0 to 9%; the main risk factor is anastomotic tension.[79] Nonfibrotic strictures at the anastomosis are common, but they respond well with anal dilatation. Fibrotic strictures may occur secondary to intraoperative complications and may more often need surgical intervention.[93] Pouch failure requiring excision (risk, 4–8%) is associated with chronic pouchitis and with pelvic leak.[55] Revision IPAA is usually possible with an acceptable outcome.[57,94] Small-bowel obstruction rate is high after IPAA; MacLean et al[95] reported a cumulative risk of 31% and need for surgical intervention in 7.5%. Pouchitis after IPAA is seen less often in patients with FAP than in patients with UC (0–11%).[79,96]

Stool frequency has been reported as four to six bowel movements daily, and average episodes of nighttime stooling were zero to one bowel movement.[92,97,98] Rates of normal daytime continence were impressively high at 80 to 95% of patients. Nighttime fecal spotting rates were moderate overall at 32 to 42%, and approximately 1% of patients reported some soiling at night.[92,98–101] Long-term follow-up in large patient populations has indicated that continence does not deteriorate significantly over time.[99,101] Pouchitis prevalence following IPAA for FAP was low (<10%).[96]

An important concern for functional outcomes is postoperative fertility, which decreases to 54% after IPAA in FAP patients.[102] Pediatric patients with FAP are often childless at the time of surgical intervention, and the desire for future fertility may be substantial.[103] IPAA does not impair childbirth or even pregnancy,[104] but it does have a considerable effect on female fertility,[102,105] as well as a small risk of impairment in male fertility.[106] A close rectal wall proctectomy technique may reduce the effect on future fertility.[104] Experts hypothesize that pelvic adhesions from the pelvic dissection may be responsible.[107,108] A subset of patients who underwent coloproctectomy with either IPAA or terminal ileostomy underwent hysterosalpingography analysis. The imaging showed unilateral or bilateral fallopian tube obstruction in 52% of patients.[109,110] Newer studies indicate that laparoscopic approaches may significantly reduce the effect of the operation on a patient's long-term fertility.[51,52]

Pregnancies are most often uneventful in patients who underwent IPAA; most pregnancies lead to term labor and delivery without complications. Neither the pregnancy nor the labor adversely affects pouch function, and there is no mandate for a Cesarean section.[70,104,111]

Urinary and sexual dysfunction is possible after IPAA, and the incidence varies depending on the rectal dissection technique.[104] With a close rectal wall dissection, minimal impact on urinary and sexual dysfunction was seen.[26,109] Colwell and Gray[106] reported rates of 0.5 to 1.5% for erectile dysfunction and 3 to 4% for ejaculatory dysfunction. Incidence of female sexual dysfunction after IPAA has been less thoroughly analyzed, but the same rates of 3 to 22% dyspareunia are reported.[112] In addition, concerns for stool leakage have led to inhibited sexual interactions in 3% of female patients after IPAA.[106]

Almost all quality-of-life outcomes after IPAA were comparable to those of healthy children.[97,99,100] In a Cleveland Clinic series, overall long-term quality of life after IPAA was rated as good to excellent in 99% of FAP patients.[101] Patient satisfaction was also markedly high after IPAA.[97,99,101] Daily activities—from social, home, travel, sports, and sexual—are affected minimally in the long term, with only 2% of patients reporting adverse outcomes in these activity areas.[113] In the pediatric setting, quality of life, physical functions, mental health, and self-esteem were all seen to be equivalent to healthy children.[97] Parental concerns about the health of the child continued to persist, however, even in the absence of physical or functional abnormalities.[97]

Conclusion

Inherited polyposis syndromes present a distinctive subset of patients whose risk of CRC may be obviated by prophylactic resection of all colorectal mucosa and IPAA reconstruction.[114] Diagnosis is becoming earlier with increasing awareness and understanding, and hence these patients are increasingly offered surgical interventions during their younger years. IPAA should be offered to the majority of patients with polyposis syndromes when their risks of colorectal malignancy have been established after serial endoscopic surveillance. The procedure is safe, results in removal of all colorectal mucosa and provides CRC risk reduction, offers good functional outcomes, and has limited complications. Continued technical advances and improved surgical techniques will likely further improve the functional outcome and patient satisfaction after IPAA.

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